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WOITACH, JOSEPH T	

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1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/885,679	PERA, MARTIN FREDERICK	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-12,14-30,37 and 45-49* is/are pending in the application.

4a) Of the above claim(s) *16-24, 28, 30 and 37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-12,14,15,25-27,29 and 45-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application filed June 20, 2001 claims benefit to foreign applications PR1327, filed November 8, 2000, and PQ8242, filed June 20, 2000, both in Australia.

Applicants' amendment filed December 8, 2003, has been received and entered. The abstract of the specification has been amended. Claims 1-3 and 13 have been canceled. Claims 4-6, 14, 15, 25, 27, 29 have been amended. Claims 45-49 have been added. Claims 4-12, 14-30, 37 and 45-49 are pending.

Election/Restriction

Applicant's election with traverse of group I, and the election of species of noggin in Paper No. 11 was acknowledged in the previous office action. No new grounds of traverse nor arguments are provided in the instant amendment.

Claims 4-12, 14-30, 37 and 45-49 are pending. Claims 16-24, 28 , 30 and 37 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 11. Newly added claims 45-49 are encompassed by the elected invention and will be examined to the extent they encompass the elected group and species. Claims 4-12, 14, 15, 25-27, 29 and 45-49 are currently under examination as they are drawn to methods of culturing ES cells with the BMP antagonist noggin.

Priority

As indicated in the prior office action, acknowledgment is made of applicant's claim for foreign priority based on applications PR1327 and PQ8242 filed in Australia on November 8, 2000 and June 20, 2000, respectively. It is noted, however, that applicant has not filed a certified copy of the Australian application as required by 35 U.S.C. 119(b). Applicants have not addressed the issue of priority nor have Applicants provided a certified copy of the applications.

Accordingly, it is maintained that the priority date of the instant application is its filing date June 20, 2001.

Specification

The abstract of the disclosure objected to because it is not present as a single paragraph is withdrawn.

The amendment to the abstract has obviated the objection.

Claim Objections

Claim 29 objected to because it was dependent on claim 28 which is a claim withdrawn from consideration is withdrawn.

The amendment to the claim has obviated the basis of the objection.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and

useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claim 25 objected to under 37 CFR 1.75 as being a substantial duplicate of claim 3 is withdrawn.

Cancellation of claim 3 has obviated the basis of the objection.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4-12, 14, 15, 25-27, 29 and 45-49

Claims 4-9 and 25-27 provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 13-15 and 20 of copending Application No. 09/670,198 is withdrawn.

The prosecution of application 09/670,198 has been abandoned, therefore, the rejection is moot.

Claims 4-12, 14, 15, 25-27, 29 and 45-49 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 13-15 and 20 of copending Application No. 10/616,682.

Prosecution of 09/670,198 has been abandoned, however 10/616,682 is a continuation of this application and contains the same claims as previously presented and discussed for 09/670,198. Specifically, although the conflicting claims are not identical, they are not patentably distinct from each other because in each case the methods are drawn to methods of culturing comprising the same steps and using noggin as an antagonist/inhibitor of the BMP pathway. Each set of claims set forth obtaining a source of pluripotential cells and the dependent claims of 10/616,682 specifically recite that ES cells are a contemplated source.

Further, each set of claims set forth inhibiting the BMP pathway, and in each application dependent claims specifically set forth that the agent used is noggin.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

To the extent that Applicants arguments apply to the instant rejection, it is noted that as with '198, '628 has not been issued, however this is not a basis for withdrawing the rejection. The assignment and inventorship between the two applications is different. Further, as detailed above the subject matter claimed in the instant application encompasses the same subject matter as '682. Applicants comments and request are not found persuasive because the two applications specifically claims the same subject matter, and accordingly a obvious double patenting rejection is appropriate (see MPEP 800, Chart I-B).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4-12, 14, 15, 25-27, 29 stand rejected and newly added 45-49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of culturing human embryonic stem (ES) cells comprising: (1) obtaining a source of human ES cells; and (2) providing culturing conditions of said human ES cells in the presence of noggin for 5 days wherein said conditions result in an undifferentiated cell which does not express ES stem

cell markers, does not reasonably provide enablement for methods using the ES cells of any species of animal or for producing progenitor cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice and make the invention commensurate in scope with these claims.

Applicants summarize the basis of rejection, and note newly added claim 45 encompassing the use of a human ES cell addressing the basis of the rejection as it is drawn to using any species of ES cells. Further, Applicants argue that the claimed methods are applicable to more that human ES cells and provide a recently published reference detailing the role of Noggin and Chordin in promoting lineage commitment in mouse ES cells, noting that noggin promoted neuronal differentiation (see page 11 and Exhibit 1). Additionally, Applicants argue that the cells produced by the instantly claimed method are fairly characterized, noting that Examiner acknowledges that noggin treated cells become neuronal and glial cells (see page 12). Applicants' arguments have been fully considered, but not found persuasive.

As stated in the previous office action, the basis of the instant rejection focuses on two main aspects of enablement. First, the ability of using and practicing the instantly claimed method in ES cells other than from those obtained from humans. Second, the nature of the resulting cells after practicing the specific method steps of culturing ES cells with an antagonist of a BMP pathway, in particular treating the cells with the elected species of noggin.

As supported by the instant specification and newly provided Gratsch *et al.* reference (exhibit 1) the affects of noggin on the BMP pathway as a neurotrophic factor were well known. As stated in the previous office action Carpenter *et al.* teach that noggin is capable of inducing dorsal development in vertebrates when expressed (column 4, lines 64-67) and that noggin is a

neurotrophic factor (column 5, lines 39-42). In the characterization of recombinant human noggin, Carpenter *et al.* demonstrate that noggin alone is capable of driving neuronal induction in developing embryos (column 25, lines 15-50; and results summarized by figures 4 and 6). Subsequently, as summarized in Shou *et al.* (Dev. 127, 5403-5413), the role of specific BMP family members and there antagonists is a complex and interactive pathway. In development, Shou *et al.* teach that "BMPs exert both ligand-specific and concentration-dependent effects on neurogenesis" and that "opposing effects (cell death and survival) are exerted at different cell stages in neuronal lineages" (page 5404, top of first column). Thus, at the time of filing, noggin was known in the art to be a neurogenic factor affecting BMP-2 and important in neuronal differentiation. Examiner does not contend that the one could not simply culture cells with noggin, nor that prolonged culturing with a neurotrophic factor would result in the formation of cells of neuronal cell lineages as this is supported by the art of record. Rather, what is supported by the present specification is that the culturing of human ES cells for 5 days provides an intermediate cell type before complete differentiation into a neuronal cell. Though generally this is not unexpected because the culturing of an undifferentiated cell into a differentiated cell must proceed through the process of differentiation providing intermediate cell types or at least phenotypes not representative of either a completely undifferentiated or differentiated cell type. However, the present specification is the first to demonstrate that culturing human ES cells for five days with noggin is sufficient to achieve this intermediate cell type, as noted in the basis of the rejection. Clearly, the art supports that prolonged culturing with noggin will result in a neuronal cell lineage (both human and mouse), at what time this happens and whether this happen at that the same time for all species of ES cells is in the basis of the rejection. As

pointed out in the previous office action, the present specification provides only a single working example wherein using human ES cells cultured in the presence of noggin for 5 days, an undifferentiated cell type lacking stem cell markers can be observed (page 28). Because of the lack of neuronal markers, the specification teaches that resulting cells are not neuronal progenitor cells (page 29, lines 15-16), however the specification acknowledges that the "identity and differentiation potential of the cells induced by treatment of human ES cells with noggin has yet to be defined" (page 29, lines 17-19). Clearly, even the teaching of the instant specification supports the Examiner's conclusions that the resulting cell type at five days is undefined. Again, one would not contend that an undifferentiated ES cell can be cultured with noggin and that ultimately a neuronal cell type. However, Applicants' arguments are not found persuasive because the art and even the guidance of the specification clearly indicates that the resulting cell intermediate cell type is undefined.

With respect to the using the methods as instantly claimed for producing "a progenitor cell", as noted above, the specification acknowledges that treating human ES cells with noggin results in a cell has not been fully characterized. Lacking neuronal cell markers the specification asserts it is not a neuronal progenitor cell. The specification provides evidence that the noggin treated human ES cell are capable of differentiating into neuronal and glial cells. Further, the specification teaches that the resulting noggin treated human ES cell can be used for a "facile route to the isolation of neuronal progenitors" (page 29, lines 13-14). In light of the lack of neuronal markers and the lack of stem cell markers, the noggin treated cell appears to be an intermediate cell type. The ability of the resulting cell to differentiate into neuronal cell types is consistent with the activity previously known and described for noggin and BMP-2. However,

based on the differences between mouse and human ES cells it can not be excluded that the human ES cell treated for 5 days with noggin results in a cell which is capable of differentiating into other somatic cell lineages besides that of neuronal origin. The courts have stated that reasonable correlation must exist between scope of exclusive right to patent application and scope of enablement set forth in patent application. 27 USPQ2d 1662 *Ex parte Maizel.* In this case, practicing the claimed methods is facile, however given the lack of characterization of the resulting noggin treated cell as acknowledged by the specification there is not objective evidence that the resulting noggin treated cell is a progenitor capable of giving rise to any somatic lineage. Given the complexity of the BMP pathway recognized in the art and the affect of noggin on ES cells from other species, the only defining character of the resulting cell considered adequately defined would be the cell lacking the original ES cell markers. As taught by the specification this noggin treated cell type can be used to produce neuronal progenitor cells.

Finally, with respect to the ability of noggin to affect any type of ES cell in culture, while it was clear from the prior art that noggin has a role and can influence development of neurons in the animals studied, Finley *et al.* (IDS reference) teaches that the ability of noggin to affect cells in culture, in particular mouse embryonic stem cells, was not directly correlative to these observations. The teachings of Gratsch *et al.* is noted, however this only supports that the affects of noggin on ES cells can be associated with neuronal cell differentiation. This is in contrast to the teaching of Finley *et al.* who report that noggin alone had no affect on the differentiation of mouse ES cells during neuronal or glial differentiation (summarized in abstract, last two lines; and detailed page 273, first column). Mehler *et al.* (Dev. Neurosci. 22:74-85) teach that role of BMPs and there antogonist is complex and progressive in affecting both differentiation and the

viability of cells during differentiation (summarized in abstract). With respect to the affects of noggin, Mehler *et al.* teach that noggin affects the percent survivability of mouse ES cells during differentiation as measured by the number of oligodendrocytes generated (figure 3). The specification provides evidence that human ES cells cultured with noggin for 5 days result in a cell which no longer expresses stem cell markers. Further, the specification demonstrates that the resulting cells are capable of differentiating into neuronal lineages, and interpreting the results it asserts that it is not simply a neuronal stem cell as evidence by the lack of neuronal markers. Clearly Finley *et al.* teach that simply supplying noggin to mouse ES cells has not affect, however the working example provided in the instant disclosure indicates that human ES cells cultured with noggin are affected. Importantly, it is known in the art that ES cells differ from species to species, in particular human ES cells differ in there *in vitro* requirements as compared to ES cells from mouse, rat or hamsters (see summary in Thomson US Pat 5,843,780, column 12, lines 40-51). Culturing human ES cells for 5 days in the presence of noggin results in a unique cell type which has not been described in other species, however given the evidence of record, it does not appear that what is observed with human ES cells will extend to any other ES cell obtained from other species. Applicants' arguments are not found persuasive because while newly supplied art supports that noggin treated mouse ES cells may become a differentiated neuronal cell type, it fails to provide any evidence of any intermediate cell type or the conditions that would produce an intermediate cell type.

In summary, the specification provides evidence that human ES cells treated with noggin for 5 days results in a cell lacking the original stem cell markers and guidance to use this resulting noggin treated cell to produce neuronal progenitor cells and potentially other cell types.

The art of record indicates that noggin may be important in differentiation into neuronal cell types, however it exact role and specific affects are still not adequately defined in mouse ES cell lines to clearly indicate that results in human ES cells would extend to the mouse. The role of noggin in human ES cells appears to be contrary to the affect of noggin in ES cells from other species and to its role in controlling neuronal differentiation. Given the guidance in the specification and the evidence of record, only methods of culturing human embryonic stem (ES) cells comprising: (1) obtaining a source of human ES cells; and (2) providing culturing conditions of said human ES cells in the presence of noggin for 5 days wherein said conditions result in an undifferentiated cell which does not express ES stem cell markers are enabled.

In view of the lack of guidance, working examples, breadth of the claims, the level of skill in the art and state of the art at the time of the claimed invention was made, it would have required undue experimentation to make and/or use the invention as claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 14, 15 and 29 stand rejected under 35 U.S.C. 102(b) as being anticipated by Thomson (US Patent 5,843,780).

Applicants note the method used to produce the instantly claimed cells and argue that Thomson fails to teach a cell type that meets the limitations of the claimed cell type. See page 14, Applicants' arguments have been fully considered, but not found persuasive.

Claims 14,15 and 29 are drawn to and encompass undifferentiated ES cells, and claims 14, 15 and 29 are drawn to and encompass a progenitor cell. Again, it is noted that a progenitor cell is not specifically defined in the specification, however within the context of the methods the term is described as a "cell which is capable of differentiation into any somatic lineage" (page 14, lines 24-26). The term "progenitor cell" as recognized in the art is a general term which is consistent with that set forth in the specification as indicated above, and for the purposes of art rejections is being interpreted by the functional ability of the cell to give rise to any somatic cell lineage. In this case, because embryonic stem cells are capable of giving rise to any somatic cell lineage, an ES cell is being interpreted to be a type of progenitor cell. Moreover, it is noted that the present specification acknowledges that even the specific cell type produced in the working example has not fully characterized. Given the limited disclosure of the cells produced by the claimed methods and the breadth of the types of cells encompassed by the terms as recognized in the art, it is maintained that the cells taught by Thomson anticipate the instantly claimed cells.

As stated in the previous office action, Thomson teach primate embryonic stem cells. The stem cells are pluripotent capable of giving rise to the various somatic cell lineages which is demonstrated by injecting the cells into a SCID mouse and analyzing the resulting cell types (column 11, lines 12-58). Thus, the anticipate the ES/progenitor cells encompassed by claims 1,

2 and 15. With respect to the specific antibody markers set forth in claim 15, it is noted that Thomoson does not specifically analyze for the presence or absence of these cell surface markers, however as recognized in the art and indicated in the present specification they represent markers on ES cell cultures which are allowed to spontaneously differentiate and are present at early time points of 7-10 days in culture (page 13, lines 20-30). Because the primate ES cells described by Thomson are highly pluripotent and not subject to differentiating conditions in culture, they would not have any of these cell surface markers. Moreover, with respect to the ES cells as claimed as a product by process (claims 13, 14, 29), where, as here, the claimed and prior art products are identical or substantially identical, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. Whether the rejection is based on "inherency" under 35 USC 102, or "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown,* 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972). With respect to the methods wherein the ES cells are cultured in the presence of noggin or where noggin is used to produce a progenitor cell, any particular affect of these methods on the ES or resulting progenitor cell to differentiate from that known in the art is not set forth. Therefore in this case, the undifferentiated ES cells and progenitor cells being claimed are being interpreted to be cells defined by their functional properties which are cells capable of giving rise to any cell type of any lineage. As noted above, Thomson teach that the primate embyronic stem cells are pluripotent and capable of giving rise to the various somatic cell lineages which was

demonstrated by injecting the ES cells into a SCID mouse and analyzing the resulting cell types (column 11, lines 12-58). Since the ES cells described by Thomson have the phenotypic characteristics of ES/progenitor cells recognized in the art as defined and supported by the instant specification, the primate ES cells described by Thomson anticipate the instantly claimed ES/progenitor cells which were cultured in the presence of noggin.

Claims 14, 15 and 29 stand rejected under 35 U.S.C. 102(e) as being anticipated by Carpenter *et al.* (Pub. No. US2002/0019046 A1).

Applicants argue that the methods used to produce the claimed cells differentiate that cells from those taught by Carpenter et al. See page 15. Applicants' arguments have been fully considered, but not found persuasive.

Claims 14 15 and 29 are drawn to undifferentiated ES cells, and claims 14, 15 and 29 are drawn to and encompass a progenitor cell, and that the term "progenitor cell" for the purposes of art rejections is being interpreted by the functional ability of the cell to give rise to any somatic cell lineage. As reasoned above, because embryonic stem cells are capable of giving rise to any somatic cell lineage, an ES cell is being interpreted to be a type of progenitor cell. Carpenter *et al.* teach primate pluripotent stem cells, and specifically teach that embryonic stem cells as taught by Thomson (page 4, paragraphs 45-48, in particular paragraph 46). Thus, to the extent that the instantly claimed products encompass embryonic stem cells, the pluripotential embryonic stem cells taught by Carpenter *et al.* anticipate claims 1, 2, 13-15 and 29.

Again, it is noted that the present specification acknowledges that even the specific cell type produced in the working example has not fully characterized. Given the limited disclosure

of the cells produced by the claimed methods and the breadth of the types of cells encompassed by the terms as recognized in the art, it is maintained that the cells taught by Carpenter *et al.* anticipate the instantly claimed cells.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Watson *et al.* Cell Structure and Function 26:123-129, (2001).

Shen The Journal of Clinical Investigations 112(4):500-502, (Aug 2003).

US Patent 6,686,198 B1, Melton et al.

Each provide further evidence of the complexity of the BMP pathway and conflicting affects of agonist and antagonists of the BMP pathway with the specific teachings of the instant specification.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (571) 272-0734.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

Joseph T. Woitach